

10/530 101

## PATENT COOPERATION TREATY

## PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT  
(PCT Article 36 and Rule 70)

RECEIVED	
06 SEP 2004	
WIPO	PCT

Applicant's or agent's file reference PU4959WO	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US 03/30334	International filing date (day/month/year) 24.09.2003	Priority date (day/month/year) 03.10.2002
International Patent Classification (IPC) or both national classification and IPC C07D471/04		
Applicant SMITHKLINE BEECHAM CORPORATION et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I  Basis of the opinion
- II  Priority
- III  Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV  Lack of unity of invention
- V  Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI  Certain documents cited
- VII  Certain defects in the international application
- VIII  Certain observations on the international application

Date of submission of the demand 05.04.2004	Date of completion of this report 02.09.2004
Name and mailing address of the international preliminary examining authority:   European Patent Office - Gitschner Str. 103 D-10958 Berlin Tel. +49 30 25901 - 0 Fax: +49 30 25901 - 840	Authorized Officer  Hoepfner, W Telephone No. +49 30 25901-337



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US 03/30334

## I. Basis of the report

1. With regard to the elements of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

### Description, Pages

1-67 as originally filed

## **Claims Numbers**

1-28 as originally filed

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
  - the language of publication of the international application (under Rule 48.3(b)).
  - the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

- 4. The amendments have resulted in the cancellation of:**

- the description, pages:
  - the claims, Nos.:
  - the drawings, sheets:

5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

- 6. Additional observations, if necessary:**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US 03/30334

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application,
- claims Nos. 17-19,23-25,28 (with respect to industrial applicability)  
because:  
 the said international application, or the said claims Nos. 17-19,23-25,28 relate to the following subject matter which does not require an international preliminary examination (specify):  
**see separate sheet**
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed:
- no international search report has been established for the said claims Nos.
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- the written form has not been furnished or does not comply with the Standard.
- the computer readable form has not been furnished or does not comply with the Standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims	6,8-13,16-22,24-28
	No: Claims	1-5,7,14,15,23
Inventive step (IS)	Yes: Claims	
	No: Claims	1-28
Industrial applicability (IA)	Yes: Claims	1-16,20-22,26,27
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US 03/30334

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 17-19, 23-25 and 28 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, the International Examination Authority fully concurs with the objection put forward by the International Search Authority and no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Reference is made to the following documents:

D1: WO-A-01014375

D2: WO-A-02072581

D3: WO-A-02048147

D4: WO-A-02048148

**Novelty**

The document D1 discloses pyrimidine derivatives of formula (I) which structurally overlap with the compounds of the present claim 1 the overlapping portion being R<sup>1</sup>=R<sup>5</sup>=H, halo, alkyl, etc.; R<sup>2</sup>=halo, alkyl etc.; R<sup>3</sup>=NR<sup>7</sup>Ay; R<sup>4</sup>=H; R<sup>7</sup>=H. The compounds of D1 are useful for the treatment of cancer (see page 1, lines 7-11, page 2, formula (I); claims 1, 10, 11).

The documents D2-D4 disclose pyrazolopyridine derivatives which structurally differ from the compounds of the present claim 1 in that there is always present a phenyl group at position 2 of the pyrazole moiety, wherein the said phenyl group is directly linked to the said pyrazole moiety. The compounds of D2-D4 are useful for the treatment of herpes viral infections (see D2: page 1, lines 5-8; page 4; formula I; Examples; D3: page 1, lines 5-8; page 5, formula I; Examples; D4: page 1, lines 5-8; page 4, formula (I); Examples).

In view of this prior art, novelty cannot be acknowledged for the subject-matter of the present independent claims 1, 14 and 23 and the present dependent claims 2-5, 7 and 15.

**Inventive step**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US 03/30334

Since it is at present not clear, on the basis of which remaining novel subject-matter the present application is to be further prosecuted, for the time being no opinion can be formulated with respect to the question, if such novel subject-matter involves an inventive step.

However, it appears at the moment that the presence of inventive activity for any possibly remaining novel subject-matter is at least questionable in view of the prior art documents D2-D4, which address the same problem, namely the provision of compounds useful for the treatment of herpes viral infections.

**Formal matters**

Although terms such as "alkyl", "alkenyl", "alkynyl" "aryl" and the like (see e.g. claim 1) are clear as such, they introduce obscurity in that they unduly extend the scope of the claimed subject-matter (breadth of the claims).

**Industrial applicability**

There is no doubt that the subject-matter of the present claims 1-16, 20-22, 26 and 27 on file is industrially applicable.

However, for the assessment of the present claims 17-19, 23-25 and 28 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims.

The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 03/30334

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7 C07D471/04 A61K31/437 A61P31/22  
 //((C07D471/04,231:00,221:00)

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
 IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, PAJ, WPI Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/014375 A (BEATTIE JOHN FRANKLIN ; BREAULT GLORIA ANNE (GB); JEWSBURY PHILLIP JOH) 1 March 2001 (2001-03-01) claims 1,10,11	1-5,7, 14,15,23
A	WO 02/072581 A (SMITHKLINE BEECHAM CORP ; BOYD F LESLIE (US); JOHNS BRIAN A (US); GUDM) 19 September 2002 (2002-09-19) page 1, line 5 - line 8 page 4, formula I Examples	1-28
A	WO 02/48147 A (GLAXO GROUP LTD ; CHAMBERLAIN STANLEY D (US); JOHNS BRIAN A (US); GUDM) 20 June 2002 (2002-06-20) page 1, line 5 - line 8 page 5, formula I Examples	1-28
		-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

\*&\* document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

13 February 2004

23/02/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
 NL - 2280 HV Rijswijk  
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
 Fax (+31-70) 340-3016

Authorized officer

Hoepfner, W

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 03/30334

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 02/48148 A (GLAXO GROUP LTD ; CHAMBERLAIN STANLEY D (US); HARRIS PHILIP ANTHONY (U) 20 June 2002 (2002-06-20) page 1, line 5 - line 8 page 4, formula (I) Examples -----	1-28

## INTERNATIONAL SEARCH REPORT

Item: application No.  
PCT/US 03/30334

### Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:

because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 17-19, 23-25 and 28 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2.  Claims Nos.:

because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3.  Claims Nos.:

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box II Observations where unity of Invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US 03/30334

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 0114375	A	01-03-2001		AT 251623 T AU 757639 B2 AU 6583300 A BG 106383 A BR 0013476 A CA 2376293 A1 CN 1370163 T CZ 20020617 A3 DE 60005850 D1 EE 200200080 A EP 1214318 A1 WO 0114375 A1 HU 0202494 A2 JP 2003507478 T NO 20020832 A SK 2402002 A3 ZA 200200028 A		15-10-2003 27-02-2003 19-03-2001 30-09-2002 30-04-2002 01-03-2001 18-09-2002 12-06-2002 13-11-2003 16-06-2003 19-06-2002 01-03-2001 28-10-2002 25-02-2003 12-04-2002 10-09-2002 02-04-2003
WO 02072581	A	19-09-2002		EP 1366048 A2 WO 02072581 A2		03-12-2003 19-09-2002
WO 0248147	A	20-06-2002		AU 3934402 A AU 3934802 A EP 1341788 A2 EP 1377573 A2 WO 0248147 A2 WO 0248148 A2		24-06-2002 24-06-2002 10-09-2003 07-01-2004 20-06-2002 20-06-2002
WO 0248148	A	20-06-2002		AU 3934402 A AU 3934802 A EP 1341788 A2 EP 1377573 A2 WO 0248147 A2 WO 0248148 A2		24-06-2002 24-06-2002 10-09-2003 07-01-2004 20-06-2002 20-06-2002